AMENDMENT AND RESPONSE UNDER 37 CFR § 1.116 - EXPEDITED PROCEDURE

Serial Number: 09/825,765 Filing Date: April 4, 2001

Title: GENETIC MODIFICATION OF ENDOSTATIN

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In the Claims

Please amend the claims as follows:

- 1. (Currently Amended) A composition consisting of a chimeric polypeptide comprising a peptide or polypeptide targeting moiety specific for endothelial cells linked to an antiangiogenic endostatin polypeptide, wherein the targeting moiety is linked to the carboxy terminus of the antiangiogenic endostatin polypeptide, and wherein the amino acid at position 125 in the endostatin polypeptide is not proline.
- 2. (Original) The composition of claim 1 wherein the targeting moiety binds to integrin on endothelial cells.
- 3. (Previously Presented) The composition of claim 2 wherein the targeting moiety comprises RGD, NGR, RGDNGR (SEQ ID NO:8), or NGRRGD (SEQ ID NO:9).
- 4. (Original) The composition of claim 2 wherein the targeting moiety binds to $_{\rm v}$ $_{\rm 3}$ / $_{\rm v}$ $_{\rm 5}$ integrins.
- 5. (Currently Amended) The composition of claim 1 wherein the targeting moiety and the anti-angiogenic endostatin polypeptide are linked via a peptide bond.
- 6-9. (Cancelled)
- 10. (Currently Amended) The composition of claim 9 1 wherein the amino acid at position 125 is alanine, valine, leucine, isoleucine or methionine.
- 11-12. (Cancelled)

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13. (Original) The composition of claim 1 further comprising a pharmaceutically acceptable diluent.

- 14. (Currently Amended) The composition of claim § 1 wherein the targeting moiety is RGD.
- 15. (Original) A sustained release dosage form comprising the composition of claim 1.
- 16. (Original) The sustained release dosage form of claim 15 which comprises alginate beads.
- 17. (Currently Amended) A host cell transformed with recombinant DNA encoding a chimeric polypeptide consisting of a peptide or polypeptide targeting moiety specific for endothelial cells linked to an antiangiogenic endostatin polypeptide, wherein the targeting moiety is linked to the carboxy terminus of the antiangiogenic endostatin polypeptide, and wherein the amino acid at position 125 in the endostatin polypeptide is not proline.
- 18. (Currently Amended) A method to inhibit or prevent undesirable endothelial cell proliferation or migration, comprising: contacting a mammalian endothelial cell with an amount of a chimeric polypeptide comprising a peptide or polypeptide targeting moiety specific for endothelial cells linked to an antiangiogenic endostatin polypeptide effective to inhibit or prevent undesirable endothelial cell proliferation or migration, wherein the targeting moiety is linked to the carboxy terminus of the antiangiogenic endostatin polypeptide, and wherein the amino acid at position 125 in the endostatin polypeptide is not proline.
- 19. (Original) The method of claim 18 wherein the mammalian cell is a human cell.
- 20. (Original) The method of claim 18 wherein the composition comprises a RGD-containing peptide linked to endostatin.

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21. (Currently Amended) A therapeutic method comprising: administering to a mammal having a condition characterized by undesirable endothelial cell proliferation or migration, a dosage from comprising an effective amount of a chimeric polypeptide comprising a peptide to polypeptide targeting moiety specific for endothelial cells linked to an antiangiogenic endostatin polypeptide, wherein the targeting moiety is linked to the carboxy terminus of the antiangiogenic endostatin polypeptide, and wherein the dosage form is a sustained release dosage form comprising alginate.

- 22. (Original) The method of claim 21 wherein the condition is cancer, diabetic retinopathy, macular degeneration, or restenosis.
- 23. (Original) The method of claim 21 wherein the condition is colon cancer.
- 24. (Original) The method of claim 21 wherein the condition is ovarian cancer.
- 25-28. (Cancelled)
- 29. (Currently Amended) The method of claim 28 21 wherein amino acid at position 125 of endostatin is not a proline.
- 30. (Original) The method of claim 29 wherein the amino acid at position 125 is alanine, valine, leucine, isoleucine or methionine.
- 31. (Previously Presented) The method of claim 18 or 21 wherein the targeting moiety is RGD, NGR, RGDNGR (SEQ ID NO:8), or NGRRGD (SEQ ID NO:9).
- 32. (Previously Presented) A composition comprising a chimeric polypeptide comprising a peptide or polypeptide targeting moiety specific for endothelial cells linked to a mutant endostatin with an amino acid substitution at position 125 or comprising a mutant endostatin with an amino acid substitution at position 125.

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33. (Previously Presented) A host cell transformed with recombinant DNA encoding a chimeric polypeptide comprising a peptide or polypeptide targeting moiety specific for endothelial cells linked to a mutant endostatin with an amino acid substitution at position 125 or encoding a mutant endostatin with an amino acid substitution at position 125.

- 34. (Previously Presented) A method to inhibit or prevent undesirable endothelial cell proliferation or migration, comprising: contacting a mammalian endothelial cell with an amount of a chimeric polypeptide comprising a peptide or polypeptide targeting moiety specific for endothelial cells linked to a mutant endostatin with an amino acid substitution at position 125 or with an amount of a mutant endostatin with an amino acid substitution at position 125, effective to inhibit or prevent undesirable endothelial cell proliferation or migration.
- 35. (Previously Presented) A therapeutic method comprising: administering to a mammal having a condition characterized by undesirable endothelial cell proliferation or migration, a dosage from comprising an effective amount of a chimeric polypeptide comprising a peptide or polypeptide targeting moiety specific for endothelial cells linked to a mutant endostatin with an amino acid substitution at position 125.